AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning at page 24, line 30 with the following rewritten paragraph:

--~~6. Figure legends~~

~~Figure 1.~~

~~Physical~~ Fig. 1 shows the physical contig and STS marker map in proximal human 8q12. The upper line indicates the chromosome, with the telomere to the left and the centromere to the right. DNA markers and genes are ordered across the top of the figure. Genes are underlined and previously known markers are indicated in bold. YAC clones are represented as lines together with their names and are described in Table 2. STS locations are indicated by dashed lines. The length of the solid line indicates its approximate size. The size of the YAC 391H2 and 392A6 is too large to fit within the constraints of the map, suggesting chimaerism. In these cases, the ~~lenght~~ length of the YAC corresponds only to the markers it contains. YAC end clones used as STS are represented as arrows. Below the contig the consensus restriction maps for BssHII (B), KpnI (K), M1uI (M), NotI (N), PvuI (P), Sa1I (S) and SfiI ~~(Sf)~~ (S) are indicated. ~~Verical~~Vertical-arrows indicate putative CpG islands, defined as the colocalization of sites for (a) K, M, N; (b) K, M, P, S, Sf; (c) K, M, P, Sf; (d) K, N, S; (e) K, N, S; (f) B, N, S; and (g) B, K, N, Sf. The pleomorphic adenoma gene region is indicated by a gray shaded box.--

Please replace the paragraph beginning at page 25, line 16, with the following rewritten paragraph:

~~--Figure 2.~~

~~Physical~~Fig. 2 shows the physical contig and STS marker map in distal human 8q12. The upper line indicates the chromosome, with the telomere to the left and the centromere to the right. DNA markers and genes are ordered across the top of the figure. Genes are underlined and previously known markers are indicated in bold. YAC clones and cosmid CEM3 are represented as lines together with their names. YAC end clones used as STS are represented by arrows.--

Please replace the paragraph beginning at page 25, line 27, with the following rewritten paragraph:

~~Figure 10.~~

Fig. 10 shows STSs used to generate the 300 kb cosmid contig mapping at chromosome 8q12 and encompassing PLAG1.--

Please replace the paragraph beginning at page 50, line 32, with the following rewritten paragraph:

~~--FIGURE LEGENDS~~

~~Figure 3~~

~~A: Contig~~Fig. 3A shows contig of 3 overlapping YACs (bold lines), 27 cosmids and 2 phages, containing 27 landmarks and spanning a 300 kb DNA region on chromosome 8q12. Contig elements are ~~labelled~~ labeled or numbered and defined in the list below. Cosmid clones isolated from the arrayed chromosome 8-specific cosmid library constructed at Los Alamos National Laboratory (LANL) (Wood et al., (1992)) are named after their unique microtiter plate addresses. ~~#1 and #22~~ No. 1 and No. 22 are genomic phage clones; ~~#21~~No. 21 is a clone isolated from the non-arrayed LANL chromosome 8-specific cosmid library. The orientation of the contig on the long arm of chromosome 8 is given as well as the order of 27 landmarks. It should be noted that the contig is not scaled. Below the contig, the genomic organization and the relative location of the PLAG1 gene is ~~given~~ shown schematically, with exact sizes (bp) of its exons and estimated sizes (kb) of its introns. Noncoding sequences are represented as open boxes and coding sequences as black boxes. The relative positions of the translation initiation (ATG) and stop (TAG) codons in PLAG1 are indicated. At the bottom of the ~~Figure~~Fig. 3A, characteristics of the deduced protein encoded by PLAG1 are given. Zinc fingers are ~~labelled~~ labeled F1-F7.--

Please replace the paragraph beginning at page 51, line 31, with the following rewritten paragraph:

--~~B: Mapping~~ Fig. 3B shows mapping of the 8q12 translocation breakpoint in an adenoma (CG644) with a t(3;8) (p21;q12). Cosmid CEM48 (white spots) was co-hybridized with alpha-satellite probes: one specific for chromosome 3 and the other for chromosome 8 (black spots). Hybridization signals were found on the normal 8, the der (3), and the der (8), indicating that CEM48 spans the t(3;8) (p21;q12) breakpoint. Chromosomes are stained in blue with DAPI.--

Please replace the paragraphs beginning at page 51, line 40 and continuing to page 52, through line 10 with the following rewritten paragraph:

--~~Figure 4~~

~~A:~~ Fig .4A shows cDNA and the deduced amino acid sequence of PLAG1. The relative positions of exon/intron boundaries are indicated by triangles (~~▼~~). The conserved C, F, L and H residues in zinc finger domains are underlined. Residues 22-25 and 29-32 constitute two potential nuclear localization signals. A potential polyadenylation signal and the putative mRNA destabilizing ATTTA motifs in the 3'-noncoding region are underlined. The nucleotide sequence of the complete cDNA has been deposited at GenBank under accession number XXX.~~B: Alignment~~Fig. 4B shows alignment of the seven zinc-finger-like motifs found in the deduced amino acid sequence of PLAG1 relative to the C2H2 consensus motif. The canonical C, F, L and H residues are given in bold.--

Please replace the paragraph beginning at page 52, line 12, with the following rewritten paragraph:

--~~Figure 5~~

~~Illustrative~~ Fig. 5 is an illustrative example of the detection of DNA rearrangement in PLAG1 of a primary pleomorphic adenoma using Southern blot analysis. DNA of pleomorphic adenoma CG368 (panel I) and control DNA isolated from normal lymphocytes (panel II) were digested with restriction endonucleases BamHI (B), EcoRI (E), HindIII (H), or PstI (P), as

indicated. A probe with specificity for exon 3 of PLAG1 (EM440) was used. The molecular weight markers are 23.1, 9.4, 6.5, 4.3, 2.3, and 2.0 kb, respectively.--

Please replace the paragraphs beginning at page 52, line 23 and continuing to page 53, through line 10 with the following rewritten paragraph:

--~~Figure 6~~

~~A:~~ Fig. 6A shows detection of CTNNB1/PLAG1 and PLAG1/CTNNB1 fusion transcripts by RT-PCR in primary adenomas. In (I), CTNNB1/PLAG1 were detected using the RT-PCR protocol and primers described in detail in the Methods. Primary tumors analyzed included CG368 (lane 1), CG588 (lane 2), CG644 (lane 3), CG682 (lane 4), CG752 (lane 5), CG753 (lane 6), T9587 (lane 7), and CG580 (lane 8). ~~H.~~ In (II), PLAG1/CTNNB1 fusion transcripts were detected similarly using the same samples as under ~~"I"~~(I). Details of the primers used here are given in the Methods Section. PCR products are ~~labelled~~labeled A-D. ~~B: Schematic~~ Fig. 6B is a schematic representation of the nature and origin of CTNNB1/PLAG1 and PLAG1/CTNNB1 fusion transcripts in primary pleomorphic adenomas with t(3;8)(p21;q12). At the top of the figure, the exon/intron distribution of the PLAG1 gene is given, at the bottom, the exon/intron distribution for the CTNNB1 gene. Positions of chromosome breakpoints are indicated by an arrow (~~▼~~). Translation initiation sites are indicated by asterisks (~~*~~) and stop codons by triangles (~~▼~~). ~~A-D:~~ Lines A-D are schematic representations of exon compositions of hybrid transcripts, as established by 5'-RACE analysis. ~~A:~~Line A is a cDNA sequence junction between exon 1 of CTNNB1 and exons 3-5 of PLAG1. ~~B:~~Line B is a cDNA sequence junction between exon 1 of CTNNB1 and exons 2-5 of PLAG1. ~~C:~~Line C is a cDNA sequence junction between exon 1 of PLAG1 and exons 2-16 of CTNNB1. ~~D:~~Line D is a cDNA sequence junction between exons 1-2 of PLAG1 and exons 2-16 of CTNNB1.--

Please replace the paragraphs beginning at page 53, line 12 and continuing to page 53, through line 30 with the following rewritten paragraph:

--~~Figure 7~~

~~A:~~ Fig. 7A is a Northern blot analysis of the expression pattern of PLAG1 in normal human fetal tissues including brain (1), lung (2), liver (3) kidney (4) as well as adult tissues

including heart (5), brain (6), placenta (7), lung (8), liver (9), skeletal muscle (10), kidney (11), and pancreas (12). ~~B:~~ Fig. 7B is a Northern blot analysis of the expression pattern of the CTNNB1 gene in normal human fetal and adult tissues as described for Fig. 7A. ~~C: Detection~~ Fig. 7C shows detection of CTNNB1/PLAG1 transcripts in pleomorphic adenomas by Northern blot analysis using exon 1 of CTNNB1 as a molecular probe. ~~Lane 1,~~Lane 1 is RNA of CG644 (t(3;8)), ~~lane 2,~~lane 2 is RNA of CG580 (t(8;15)), and ~~lane 3,~~lane 3 is RNA of CG682 (ins 3p21(8q12)). The CTNNB1/PLAG1 fusion transcript is indicated. ~~D:~~ Using the same blot as under ~~"C",~~ Fig. 7C, Fig. 7D shows detection of CTNNB1/PLAG1 transcripts using a probe with specificity for the 3' UTR of PLAG1 (probe KK64). The CTNNB1/PLAG1 ~~tran script~~transcript is indicated.--